DETAILED ACTION

1. Acknowledgment is made of Applicant's Response, which was received by the Office on May 21, 2008. In response to Applicant's note of "the absence of the mention of pending claims 4-7, 14-31, 35-38, 45-62 and 79-148" in the Restriction Requirement of April 21, 2008 (see page 22 or the Remarks), the Examiner respectfully directs Applicant's attention to page 2, paragraph 1 of the Restriction Requirement where the Examiner noted Applicant's submission of February 20, 2008 and explicitly summarized the status of such previously withdrawn claims.

Election/Restrictions

2. Applicant's election with traverse of Group I (claims 1-3, 10-13, 150 and 151) in the reply filed on May 21, 2008 is acknowledged. The traversal is on the ground(s) that "Restriction Requirements are optional in all cases" and there is no additional burden placed on the Examiner because claims 1-3, 10-13, 32-34, 41-44, 63-78, 150 and 151 "have been searched and examined" (see page 22 or the Remarks filed May 21, 2008). This is not found to be persuasive.

3. Applicant's submission of February 20, 2008 included amendment(s) to Claim 32 adding new limitations of a "user input device" and "an external controller". 37 CFR 1.142(a) provides that restriction is proper at any stage of prosecution up to final action and per MPEP § 811, a proper requirement should be made as early as possible in prosecution, "in the first action if possible, otherwise, as soon as the need for a proper requirement develops". As detailed in the Restriction Requirement of April 21, 2008 (herein "the recent RR"), Group I (claims 1-3, 10-13, 150 and 151) and Group II (claims 32-34, 41-44, 63-78, 150 and 151) are related as combination and subcombination, in view of Applicant's submission of February 20, 2008. Restriction is proper between combination and subcombination inventions when two-way distinctness exists between the inventions and if reasons for insisting on restriction as necessary are present (i.e., there would be a serious search burden if restriction were not required as evidenced by separate classification, status, or field of search). See MPEP § 806.05(c). At pages 2-3, paragraph 3 of the recent RR, the Examiner effectively established two-way distinctness between Groups I and II by showing that the combination as claimed (Group I) does not require the particulars of the subcombination as claimed (Group II) for patentability, and that the subcombination (Group II)

has utility by itself or in other combinations. As discussed at pages 3-4, paragraph 4 of the recent RR, there would be a serious search and examination burden if restriction were not required because the inventions have acquired a separate status in the art and because the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries). See MPEP § 808.02. Applicant has not provided any evidence and/or convincing rationale showing that the inventions of Groups I and II are not distinct, nor has Applicant effectively shown that there would not be a serious search and examination burden if restriction between Groups I and II was not required. Applicant argues that "claim 1 is believed to be a generic to claim 32" and therefore, "a search and examination of claim 1 would include a search and examination of claim 32", however, as discussed at pages 2-3, paragraph 3 of the recent RR, the combination as claimed (Group I) does not require the details of the subcombination as claimed (II), therefore, a search of the combination would not necessarily include the details of the subcombination.

4. The requirement is still deemed proper and is therefore made FINAL. Claims 32-34, 41-44, 63-78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Information Disclosure Statement

5. The information disclosure statements submitted on February 20, 208, March 17, 2008 and May 21, 2008 have been acknowledged and are being considered by the Examiner.

6. Applicant should note that the large number of references (both previously and newly submitted) have been considered by the Examiner in the same manner as other documents in Office search files are considered by the Examiner while conducting a search of the prior art in a proper field of search. See MPEP § 609.05(b). As previously requested in the Non-Final Rejection of April 26, 2007 and in the Final Rejection of December 4, 2007, Applicant is again respectfully requested to point out any particular references which they believe may be of particular relevance of the instant claimed invention. Applicant is respectfully advised that the MPEP states the following with respect to large information disclosure statements:

> Although a concise explanation of the relevance of the information is not required for English language information, Applicants are encouraged to provide a concise explanation of why the English-language information is being submitted and how it is understood to be relevant. Concise

> explanations (especially those which point out the relevant pages and lines) are helpful to the Office, particularly where documents are lengthy and complex and Applicant is aware of a section that is highly relevant to patentability or where a large number of documents are submitted and Applicant is aware that one or more are highly relevant to patentability MPEP § 609.04(a).

7. This statement is in accord with dicta from *Molins PLC v. Textron, Inc.*, 48 F.3d 1172 (Fed. Cir. 1995), stating that forcing the Examiner to find "a needle in a haystack" is "probative of bad faith." *Id.* at 1888. This case presented a situation where the disclosure was in excess of 700 pages and contained more than fifty references. *Id* 1888. The MPEP provides more support for this position. In a subsection entitled "Aids to Compliance With Duty of Disclosure," item thirteen states:

> It is desirable to avoid the submission of long lists of documents if it can be avoided. Eliminate clearly irrelevant information and marginally pertinent cumulative information. If a long list is submitted, highlight those documents which have been specifically brought to Applicant's attention and/or are known to be of the most significance. See Penn Yan Boats, Inc. v. Sea Lark Boats, Inc., 359 F.Supp 948 (S.D. Fla. 1972). aff'd 479 F.2d 1338 (5thCir 1974). MPEP § 2004.

8. Therefore, it is recommended that if any information that has been cited by Applicants is known to be material for patentability as defined by 37 CFR 1.56, Applicant should present a concise statement as to the relevance of that/those particular documents in an effort to expedite prosecution of the current application.

Claim Rejections - 35 USC § 102

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

10. ***Claims 1, 2, 13, 150 and 151 are rejected under 35 U.S.C. 102(a) and under 35 U.S.C. 102(e) as being anticipated by Padua et al. (U.S. 2003/0204206) (herein Padua).*** As to Claims 1, 2 and 13, Padua expressly discloses a system 22 for controlling and regulating production of therapeutic products comprising one or more sensors (i.e. intracardiac electrogram sensing electrodes, a subcutaneous electrode array, blood gas sensors, pH sensors, blood flow sensors etc.) for sensing physiological signals indicative of predetermined cardiac conditions (i.e. ischemia or reduced blood flow onset) and a sensing element, read as an event detector 17 adapted to detect the predetermined cardiac condition (i.e. ischemia or reduced blood flow onset) from one or more of the sensed physiological signals and adapted to produce one or more

conditions parameters related to the type of the predetermined condition where the conditions parameters (i.e. ST segment elevation or reduction of blood blow in the coronary sinus) are used in a closed-loop control algorithm of the system 22(see Padua Figs. 11 and 12, page 11, paragraphs 162 and 164, page 12, paragraphs 170-171 and 173 and page 13, paragraphs 181-183). The system 22 of Padua further comprises a gene regulatory signal delivery device (output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12) that emits, in response to a gene regulatory control signal, an electric fieldas a regulatory signal which regulates transcription from a regulatable transcriptional control element (i.e. an electrically responsive promoter (ERP)) in an expression vector (i.e. a plasmid, adenovirus vector, retrovirus vector or the like) having the regulatable transcriptional control element operably linked to an open reading frame, the expression of which treats the predetermined cardiac condition. Padua expressly discloses that the system 22 provides for introducing into at least one cell of a patient, a vector containing an electrically responsive element (ERE) operably linked to a promoter to form an electrically responsive promoter (ERP) that modulates transcription of an operably linked therapeutic product in a cell upon delivery of the regulatory signal. Padua further discloses that the genetically engineered ERP is operably linked to a therapeutic gene sequence, the expression of which is controlled by the electric fieldregulatory signal emitted by the gene regulatory delivery device of the system 22 (see Padua page1, paragraphs 1-9, page 2, paragraphs 11-12, pages 3-6, paragraphs 59-105, pages 8-10, paragraphs 117-144, page 11, paragraphs 156-161 and page 13, paragraphs 177-180).

A controller (micro-processor and memory circuitry 15 of Padua Fig. 11 or microcomputer unit 78 of Padua Fig. 12) is coupled to the one or more sensors (see, for example, sense amplifier 53 or electrogram amplifier 76 of Padua Fig. 12) and is electrically connected to the gene regulatory signal delivery device (either output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12) for producing the gene regulatory control signal (such as trigger signal provided by digital controller/timer circuit 92). In particular, the controller of the system 22 is adapted to produce a gene regulatory control signal for quantitatively controlling and regulating the electric field regulatory signal emitted (by either output circuit 12 or output pulse generator 74). The quantitative control may be triggered by a patient activator or automatically based on the determined one or more condition parameters (i.e. ST segment

elevation or reduction of blood blow in the coronary sinus) (see Padua page 12, paragraph 173). Padua specifies that the system 22 provides "controlled delivery of therapeutic gene products" and that electric field regulatory signal emitted by the gene regulatory signal delivery device of the system 22 "is used to closely modulate the time, frequency, and delivery amount of a given therapeutic product". The emitted electric field regulatory signal is specifically used as a means to control the expression of ERPs that have been transplanted or incorporated into the tissue of a mammal and "controlled expression" is controlled by closely regulating the emitted electric field regulatory signal through use of the system's controller (see Padua page 1, paragraph 5). In particular, the triggered regulatory control signal may include parameters that quantitatively control emission of the electric field regulatory signal where the parameters include predetermined timing and wave shape parameters for providing a "therapeutically effective amount" or "pharmacologically effective stimulus" (see Padua page 5, paragraphs 84 and 88-91, page 9, paragraphs 131-135, page 11, paragraphs 156-161, page 13, paragraphs 179-180 and page 14, paragraph 202).

11. As to Claim 150, in addition to the arguments previously presented, in some embodiments of Padua, the vector is not "part of an implantable device". Padua expressly discloses that the ERP constructs can be delivered directly to tissues of cells of the patient in vivo through the use of an appropriate gene delivery vector (viral or non-viral) through direct injection into the target tissue or through intravenous injection through a catheter (see Padua page 1, paragraph 5 and pages 9-10, paragraphs 131-144).

12. As to Claim 151, in addition to the arguments previously presented, the controller comprises a timer circuit (see Padua Fig. 12 and page 12, paragraph 168) adapted to time a predetermined time period of delivery time during which the gene regulatory signal delivery device emits the regulatory signal/signals (i.e. when a triggering event occurs, as previously discussed). Padua expressly discloses that the controller of the system 22 is used to closely modulate the time, frequency and delivery amount of the therapeutic product and the locus of delivery and specifies that delivery of the therapeutic product can be controlled by the location of the electrodes and the period of electrical stimulation (see Padua page 1, paragraph 5 and page 9, paragraph 136). The triggered regulatory signals are quantitatively regulated through

predetermined timing and wave shape parameters defined by the controller and its timer circuit (see Padua page 12, paragraphs 172-173).

13. ***Claims 10-12 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as anticipated by Padua or, in the alternative, under 35 U.S.C. 103(a) as obvious over Padua in view of Donahue et al. (U.S. 2002/0155101) (herein Donahue).*** In addition to the arguments previously presented, Padua expressly discloses that implantable pulse generators that are well known in the art may be modified to stimulate the injected/implanted/introduced ERP-cells in accordance with the teachings of the implantable medical device system 22 of Figs. 11 and 12 including a wide variety of microprocessor based implantable pacemakers and implantable pacemaker/cardioverter/defibrillators (see Padua page 11, paragraph 166). A plurality of the implantable pacemakers and implantable pacemaker/cardioverter/defibrillators cited by Padua at page 11, paragraph 166 include event detection circuitry which comprise atrial and ventricular fibrillation detectors such as Bardy (U.S. 5,314,430).

Furthermore, Donahue teaches that it is well known in the art to use a regulatable transcriptional control element in cardiac gene therapy for treatment of any of the following: sinus bradycardia, sinus tachycardia, atrial tachycardia, atrial fibrillation, atrial flutter, atrioventricular nodal block, atrioventricular node reentry tachycardia, atrioventricular reciprocating tachycardia, ventricular tachycardia or ventricular fibrillation (see Donahue page 7, paragraph 94). Donahue also discloses that practice of the invention is broadly compatible with one or a combination of different administration systems (see Donahue page 7, paragraph 88) for more effective and flexible anti-arrhythmic therapies by providing therapeutic methods for administering one or more therapeutic polynucleotides to the heart under conditions sufficient to modulate (increase or decrease) at least one heart electrical property. Donahue further discloses that the invention modulates heart electrical conduction, reconfigures all or part of the cardiac action potential (AP) and reduces or avoids significant disruption of normal electrical function (see Donahue page 2, paragraph 14). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Padua in view of Donahue to administer the gene therapy upon detection of an atrial fibrillation or ventricular fibrillation to better the system's capabilities of eliminating a wide variety of predetermined cardiac conditions.

Claim Rejections - 35 USC § 103

14. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

15. ***Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Padua.*** Padua discloses the essential features of the claimed invention except that it is not specified that the gene regulatory signal delivery device emit an electromagnetic field regulatory signal. Instead, as previously discussed, the gene regulatory signal delivery device of the system 22 (either output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12) is coupled to unipolar or bipolar electrodes for forming an electric field generator that emits an electric field as the gene regulatory signal for controlling and regulating the ERP (see, for example, Padua page 2, paragraph 21, page 3, paragraph 60, page 10, paragraphs 145-150 and page 13, paragraph 179).

At the time the invention was made, it would have been an obvious matter of design choice to a person of ordinary skill in the art to modify the gene regulatory signal delivery device of the system taught Padua such that it comprises an electromagnetic field generator for emitting an electromagnetic field as the gene regulatory signal, because Applicant has not disclosed that such modification provides an advantage, is used for a particular purpose or solves a stated problem. Furthermore, the Examiner considers electromagnetic field generators for emitting electromagnetic fields as gene regulatory signals to be conventional and well known in the art of gene therapy for regulating gene expression. The Examiner cites Goodman et al. (U.S. 2002/0099026), Kaplitt et al. (U.S. 2003/0087264) and Brighton (U.S. 2004/0073260) as just three examples. Accordingly, one of ordinary skill in the art would have expected the system of Padua, and Applicant's invention, to perform to perform equally well with the emitted electric field gene regulatory signal as taught by Padua or the claimed electromagnetic field gene regulatory signal, because both signals would perform the same function of controlling and regulating gene expression in a patient via electrical devices equally well. Therefore, it would have been prima facie obvious to modify Padua to obtain the invention as specified in Claim 3 because such a modification would have been considered a mere design consideration which fails to patentably distinguish over the prior art of Padua.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. ***Claims 1-3, 10-13, 150 and 151 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36, 38-78, 96-111 of copending Application No. 10/890,825 (Amended February 22, 2008) in view of Padua.*** Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof. As to Claim 1 of the current application, Application No. 10/890,825 also claims an implantable medical system, comprising a sensor to sense a physiological signal indicative of a predetermined cardiac condition, an event detector, coupled to the sensor, to detect the predetermined cardiac condition from the physiological signal, an

implant telemetry module to receive an external command and an implant controller coupled to the event detector and the implant telemetry module, the implant controller including a gene or protein delivery control module adapted to produce an electrical signal to control gene or protein delivery in response to the predetermined cardiac condition and the external command. Similar analysis may be applied to the remaining dependent claims of the current application upon inspection of the conflicting and pending claims 1-36, 38-78, 96-111 of copending Application No. 10/890,825.

The co-pending application includes synonymous limitations, as discussed, except does not specify that the protein delivery be provided by a regulatable transcriptional control element (i.e. an electrically responsive promoter (ERP)) in an expression vector (i.e. a plasmid, adenovirus vector, retrovirus vector or the like) having the regulatable transcriptional control element operably linked to an open reading frame, the expression of which produces the protein. Padua, however, teaches that the use of such ERP-cells is conventional and known in the art for providing selective and regulated gene therapy in a patient (see those sections of Padua cited above in this Office Action). Therefore, it would have been obvious to one having ordinary skill in the art, at the time the invention was made, to modify the claims of co-pending Application No. 10/890,825 such that the protein production is provided by an electrically responsive promoter (ERP) in an expression vector having the ERP operably linked to an open reading frame, the expression of which produces the protein, as taught by Padua, since such a modification would provide selective and regulated gene therapy.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. ***Claims 1-3, 10-13, 150 and 151 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 of copending Application No. 11/220,397.*** Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof. As to Claim 1 of the current application, Application No. 11/120,397 also claims a sensing circuit to sense one or more parameters indicative of an ischemic event, an ischemia detector, coupled to the sensing circuit, to detect the ischemic event from the one or more parameters, a gene regulatory signal delivery

device adapted to emit at least one gene regulatory signal that regulates transcription from a regulatable transcriptional control element within a vector and operably linked to an open reading frame and a controller coupled to the ischemia detector and the gene regulatory signal delivery device, the controller adapted to quantitatively control the emission of the regulatory signal from the gene regulatory signal delivery device. Similar analysis may be applied to the remaining dependent claims of the current application upon inspection of the conflicting and pending claims 1-31 of copending Application No. 11/120,397.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. ***Claims 1-3, 10-13, 150 and 151 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of copending Application No. 11/276,077.*** Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof. As to Claim 1 of the current application, Application No. 11/276,077 also claims a sensing circuit to sense one or more parameters indicative of an event, a gene regulatory signal delivery device adapted to emit at least one gene regulatory signal that regulates transcription from a regulatable transcriptional control element within a vector and operably linked to an open reading frame and a controller coupled to the ischemia detector and the gene regulatory signal delivery device, the controller adapted to quantitatively control the emission of the regulatory signal from the gene regulatory signal delivery device. Similar analysis may be applied to the remaining dependent claims of the current application upon inspection of the conflicting and pending claims 1-41 of copending Application No. Application No. 11/276,077.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

20. Applicant's arguments with respect to Claim 1, filed February 20, 2008, have been fully considered but they are not persuasive. Applicant argues that Padua fails to disclose a controller "adapted to produce a gene regulatory control signal including parameters that quantitatively

control the emission of the regulatory signal based on the one or more condition parameters" (see page 22 or the Remarks filed February 20, 2008). The Examiner respectfully disagrees. Although the parameters of Padua may be "predetermined", such predetermined parameters are used to *quantitatively* control and regulate the electric field regulatory signal for subsequently controlling and regulating the delivery of therapeutic gene products (emphasis added). The quantitative control is triggered, and is therefore, based on the event detector determined one or more condition parameters. As previously discussed above in this Office Action, Padua discloses that the controller of the system 22 is adapted to produce a gene regulatory control signal for quantitatively controlling and regulating the electric field regulatory signal emitted (by either output circuit 12 or output pulse generator 74). The quantitative control may be triggered by a patient activator or automatically based on the determined one or more condition parameters (i.e. ST segment elevation or reduction of blood blow in the coronary sinus) (see Padua page 12, paragraph 173). Padua specifies that the system 22 provides "controlled delivery of therapeutic gene products" and that electric field regulatory signal emitted by the gene regulatory signal delivery device of the system 22 "is used to closely modulate the time, frequency, and delivery amount of a given therapeutic product". The emitted electric field regulatory signal is specifically used as a means to control the expression of ERPs that have been transplanted or incorporated into the tissue of a mammal and "controlled expression" is controlled by closely regulating the emitted electric field regulatory signal through use of the system's controller (see Padua page 1, paragraph 5). In particular, the triggered regulatory control signal may include parameters that quantitatively control emission of the electric field regulatory signal where the parameters include predetermined timing and wave shape parameters for providing a "therapeutically effective amount" or "pharmacologically effective stimulus" (see Padua page 5, paragraphs 84 and 88-91, page 9, paragraphs 131-135, page 11, paragraphs 156-161, page 13, paragraphs 179-180 and page 14, paragraph 202).

Conclusion

21. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure.

22. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JESSICA REIDEL whose telephone number is (571)272-2129. The Examiner can normally be reached on Monday - Friday, 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Carl H. Layno can be reached on (571)272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jessica L. Reidel/
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